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10/673,575	09/30/2003	Sudhir K. Sinha	P56885	2640

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EXAMINER	
BABIC, CHRISTOPHER M	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 05/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/673,575	SINHA ET AL.	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-9,21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7-9,21 and 22* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *9/30/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1, 5-9, 21, and 22 are pending. The following Office Action is in response to Applicant's response dated April 10, 2006. Upon further consideration, the finality of the rejection of the last Office action is withdrawn.

Claim Rejections - 35 USC § 102

Upon further consideration, a new ground(s) of rejection is made in view of newly discovered applicable prior art.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Keller et al. ("Molecular evolution of the CMT1A-REP region: a human- and chimpanzee-specific repeat. Mol Biol Evol. 1999 Aug;16(8):1019-26").

With regard to Claim 1, it is initially noted that the phrase --for quantitating a human DNA in a sample-- is considered an *intended use* of the method and does not incorporate a patentably distinct feature.

Keller et al. teach a method (pages 1020, 1021, materials and methods, for example) comprising: providing a sample to be analyzed (page 1020, materials and methods, non-human primate samples, for example); amplifying predetermined genomic DNA containing an Alu element by using primers (figure 1, primers P1/C1, P2/T1, D1/C1, T1/D2; pages 1020, 1021, materials and methods, polymerase chain reaction, for example), said Alu element being enriched in the human genome (page 1023, figure 3c, lane hu, for example) compared to non-human primates genomes (page 1023, figure 3c, lanes go-ga, for example); the amplification being intra-Alu polymerase chain reaction amplification (figure 1, primers P1/C1, P2/T1, D1/C1, T1/D2; pages 1020, 1021, materials and methods, polymerase chain reaction, for example); and quantitating the human DNA by comparing the amplified DNA with a reference (page 1023, figure 3c).

With regard Claim 7, Keller teaches detecting the human DNA on an agarose gel stained with ethidium bromide (Page 38, Column 2, Paragraph 1).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 1 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434) in view of Brooks-Wilson et al. ("Human repeat element-mediated PCR: cloning and mapping of chromosome 10 DNA markers" Genomics. 1992 Jun;13(2):409-14).

Regarding Claim 1, Palmirotta et al. disclose a process for quantitating a human DNA in a sample, said process comprising the steps of: providing a sample to be analyzed (Page 432, Column 2, Paragraphs 2,3); amplifying predetermined genomic DNA containing an Alu element by using primers (Page 432, Column 2, Paragraph 3) said Alu element being enriched in the human genome (Figure 1, Lane1) compared to non-human primates genomes (Figure 1, Lanes 9-15); and quantitating the human DNA

by comparing the amplified DNA with a reference (Figure 1). Palmirotta et al. does not specifically disclose the practice of an *intra*-ALU PCR.

Brooks-Wilson et al. teaches a method of intra-Alu PCR (i.e. Alu element-mediated PCR) for amplification of human sequences (page 615, PCR amplification of human sequences, for example). Brooks-Wilson further discloses several advantages of Alu element-mediated PCR over conventional methods for isolating human sequences from mixed DNA samples such as allowing access to sequences that may be underrepresented in traditional DNA libraries (page 618, column 2, paragraph 3, for example). They further disclose that Alu element-mediated PCR abrogates the time-consuming screening for human sequences (page 618, column 2, paragraph 1, for example).

It would have been *prima facie* obvious to a practitioner ordinary skill in the art at the time of invention to incorporate intra-Alu PCR into the methods of Palmirotta since Brooks-Wilson suggests such a modification for among other reasons, to allow access to sequences that may be underrepresented in traditional DNA libraries

Regarding Claim 7, Palmirotta et al. disclose detecting the human DNA on an agarose gel stained with ethidium bromide (Figure 1).

2. Claims 1, 7, 21, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Brooks-Wilson et al.

("Human repeat element-mediated PCR: cloning and mapping of chromosome 10 DNA markers" Genomics. 1992 Jun;13(2):409-14).

Regarding Claim 1, Carroll et al. disclose a process for quantitating a human DNA in a sample, said process comprising the steps of: providing a sample to be analyzed (Page 38, Column 1, Paragraphs 2); amplifying predetermined genomic DNA containing an Alu element by using primers (Page 38, Column 2, Paragraph 1) said Alu element being enriched in the human genome (Abstract) compared to non-human primates genomes (Abstract); and quantitating the human DNA by comparing the amplified DNA with a reference (Page 38, Column 2, Paragraph 1). Carroll et al. does not specifically disclose the practice of an intra-ALU PCR.

Brooks-Wilson et al. teaches a method of intra-Alu PCR (i.e. Alu element-mediated PCR) for amplification of human sequences (page 615, PCR amplification of human sequences, for example). Brooks-Wilson further discloses several advantages of Alu element-mediated PCR over conventional methods for isolating human sequences from mixed DNA samples such as allowing access to sequences that may be underrepresented in traditional DNA libraries (page 618, column 2, paragraph 3, for example). They further disclose that Alu element-mediated PCR abrogates the time-consuming screening for human sequences (page 618, column 2, paragraph 1, for example).

It would have been *prima facie* obvious to a practitioner ordinary skill in the art at the time of invention to incorporate intra-Alu PCR into the methods of Carroll since

Brooks-Wilson suggests such a modification for among other reasons, to allow access to sequences that may be underrepresented in traditional DNA libraries.

Regarding Claim 7, Carroll teaches detecting the human DNA on an agarose gel stained with ethidium bromide (Page 38, Column 2, Paragraph 1).

Regarding Claim 21, Carroll teaches a process for quantitating a human DNA in a sample, said process comprising the steps of: providing a sample to be analyzed (Page 38, Column 1, Paragraphs 2); amplifying predetermined genomic DNA containing an Alu element by using primers (Page 38, Column 2, Paragraph 1), said Alu element being present only in the human genome (Abstract); and quantitating the human DNA by comparing the amplified DNA with a reference (Page 38, Column 2, Paragraph 1). Please refer to the rejection of Claim 1 for the discussion of intra-Alu PCR.

Regarding Claim 22, Carroll teaches a process for quantitating a human DNA in a sample, said process comprising the steps of: providing a sample to be analyzed (Page 38, Column 1, Paragraphs 2); amplifying predetermined genomic DNA containing an young Alu element by using primers (Page 38, Column 2, Paragraph 1), said young Alu element being largely absent from non-human primates (Abstract); and quantitating the human DNA by comparing the amplified DNA with a reference (Page 38, Column 2, Paragraph 1). Please refer to the rejection of Claim 1 for the discussion of intra-Alu PCR.

3. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their

Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Brooks-Wilson et al. ("Human repeat element-mediated PCR: cloning and mapping of chromosome 10 DNA markers" Genomics. 1992 Jun;13(2):409-14), in further view of Jurka ("A new subfamily of recently retroposed human Alu repeats" Nucleic Acids Research. 1993. Vol. 21. No. 9, Page 2252), and Buck et al. ("Design Strategies and Performance of Custom DNA Sequencing Primers") BioTechniques. September 1999. 27: Pages 528-536).

Regarding Claim 5, the methods of the previously applied references have been outlined in the above rejections. The previously applied references do not expressly disclose the *exact* primer sequences of SEQ ID NO: 3 and SEQ ID NO: 4, drawn to the Yb8 Alu subfamily.

Jurka discloses the entire Sb2 Alu subfamily sequence (Figure 1). The term "Sb2" is considered to older nomenclature of the Yb8 subfamily (See reference: Batzer et al. "Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, Pages 3-6).

The *identical* sequence presented in SEQ ID NO: 3 (5'-CGAGGCGGGTGGATCATGAGGT-3' is contained in the sequence provided by Jurka (Figure 1) from nucleotides 48-69. Furthermore, the *identical* complement of the sequence (i.e. reverse primer) presented in SEQ ID NO: 4 (5'-TCTGTCGCCCAGGCCGGACT -3' is contained in the sequence provided by Jurka (Figure 1) from nucleotides 273-254.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties"

Since the claimed primers simply represent complementary functional homologues of the sequences taught by Jurka, the claimed primers are *prima facie* obvious over Jurka in view Buck et al.

Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing

analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

5. Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434) in view of Brooks-Wilson et al. ("Human repeat element-mediated PCR: cloning and mapping of chromosome 10 DNA markers" Genomics. 1992 Jun;13(2):409-14), in view of Gelmini et al. ("Quantitative polymerase chain reaction-based homogeneous assay with fluorogenic probes to measure c-*erb*B-2 oncogene amplification" Clinical Chemistry. 1997. 43:5, Pages 752-758).

Regarding Claims 8 and 9, the methods of the previously applied references have been outlined in the above rejections. The previously applied references do not specifically disclose the practice of a quantitative PCR system such as *Taq*Man.

Gelmini et al. disclose the practice of a quantitative PCR system using *Taq*Man chemistry (Figures 1,2,3; Table 1; Page 754, Columns 1,2). Furthermore, they highlight

the advantages of using fluorogenic probes in PCR, such as the circumventing of post-PCR product quantitation procedures (Page 752, Column 2, Paragraph 2).

It would have been *prima facie* obvious to a practitioner ordinary skill in the art at the time of invention to incorporate a quantitative PCR system into the methods of Palmirotta since Gelmini suggests such a modification for among other reasons, to circumvent post-PCR product quantitation procedures.

6. Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carroll et al. ("Large-scale Analysis of the Alu Ya5 and Yb8 Subfamilies and their Contribution to Human Genomic Diversity" Journal of Molecular Biology. 2001. 311, Pages 17-40) in view of Brooks-Wilson et al. ("Human repeat element-mediated PCR: cloning and mapping of chromosome 10 DNA markers" Genomics. 1992 Jun;13(2):409-14), in view of Gelmini et al. ("Quantitative polymerase chain reaction-based homogeneous assay with fluorogenic probes to measure c-*erb*B-2 oncogene amplification" Clinical Chemistry. 1997. 43:5, Pages 752-758).

Regarding Claims 8 and 9, the methods of the previously applied references have been outlined in the above rejections. The previously applied references do not specifically disclose the practice of a quantitative PCR system such as *Taq*Man.

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the advantages of using fluorogenic probes in PCR, such as the circumventing of post-PCR product quantitation procedures (Page 752, Column 2, Paragraph 2).

It would have been *prima facie* obvious to a practitioner ordinary skill in the art at the time of invention to incorporate a quantitative PCR system into the methods of Carroll since Gelmini suggests such a modification for among other reasons, to circumvent post-PCR product quantitation procedures.

Allowable Subject Matter

Claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicants' arguments with regard to the previous rejection of Claim 6, upon further consideration, are persuasive. None of the previously applied references teach or suggest the amplification of the AluYd6 subfamily of human specific Alu elements. The sequences presented in SEQ ID NOs: 5 and 6 are novel and unobvious over the prior art.

Response to Arguments- 35 USC § 103

All Applicants' arguments remaining relevant to the current rejections will be addressed in the following response.

With regard to the Palmirotta reference, Applicant asserts that the quantitation step is neither taught nor suggested. It is initially noted that the phrase --quantitating

the human DNA by comparing the amplified DNA with a reference-- is broad in nature with respect to applicable prior art and is being intrepreted as such. The Examiner continues to maintain that Claim 1 recites *quantitation by comparison* with a reference, which is clearly encompassed by the visual comparison one can make with an ethidium stained gel. Figure 1 of Palmirotta et al. clearly demonstrates a visual comparison with an ethidium stained gel. Carroll et al. disclose detecting the human DNA on an agarose gel stained with ethidium bromide (Page 38, Column 2, Paragraph 1). In other words, ethidium stained gels show, based on fluorescence, that one lane has a greater or lesser *quantity* of DNA than another. Claim 1 one does not require that specific units of measurement determined with processes such as quantitative PCR. Thus, in a broader sense, agarose gel electophoresis is a quantitative procedure. Moreover, Claim 7 of the instant application recites the quantitation step of the independent method as comprising detecting the human DNA on an agarose gel stained with ethidium bromide. The Examiner understands that Claim 7 is read as incorporating ~~the~~ all the limitations of Claim 1, however, this means that the quantitation step of Claim 1 can be read as comprising *only* the step of detecting the human DNA on an agarose gel stained with ethidium bromide and comparing the DNA with a reference. A stated above, ethidium stained gels show, based on fluorescence, that one lane has a greater or lesser *quantity* of DNA than another.

Applicant further asserts that Palmirotta fails to show ~~a~~said Alu element being enriched in the human genome compared to non-human primate genomes. Applicant further argues that it cannot be determined whether the statue blood originated from

humans of from a non-human catarrhine primate. First, whether it can be determined whether the statue blood originated from humans of from a non-human catarrhine primates is irrelevant to the above feature recited in Claim 1. Furthermore, the results of Palmirotta clearly show that while Alu PCR product was obtained from human samples (page 432, column 2, results; figure 1, lane 2), no Alu PCR was obtained in New World monkey Saimiri sciurerus (page 432, column 2, results; figure 1, lane 7). The above feature recited in Claim 1 does not require the Alu element being absent from *every* non-human primate genome. Thus, these results clearly demonstrate an Alu element being enriched in the human genome compared to non-human primate genomes.

With regard to the Carroll reference, Applicant asserts that the quantitation step is neither taught nor suggested. Please refer to the related responses above.

With regard to the rejection of Claims 8 and 9, Applicant asserts that there is no suggestion or motivation to combine reference teachings. Applicant argues that since the purposes of the above references are not related to the quantitation step, there is no reason to perform a quantitation step in view of Gelmini. First, the purposes of the applied references are irrelevant to the specific disclosure of active method steps. The references teach and/or suggest every aspect of the claimed invention.

Conclusion

Claims 1, 5, 7-9, 21, and 22 are rejected.

Claim 6 is objected to.

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Sifis et al. ("A more sensitive method for the quantitation of genomic DNA by Alu amplification. J Forensic Sci. 2002 May;47(3):589-92").

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

5/8/06

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KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

5/11/06